

of a biopharmaceutical company. An approach based on real options valuation model was proposed to support investment and market decisions and to predict the potential net present value (NPV) of a drug. The conceptual structure of the model was face-validated by health economic and valuation experts. **RESULTS:** A decision-tree based valuation method, populated partially by information from health economic tools, was adopted to analyse and clearly communicate R&D investment opportunities, to capture management flexibility and to improve strategic thinking. A feedback loop can be built into the model to analyse resiliency to assumption changes. In early phases, headroom and multi-criteria decision analyses indicate the likelihood of an investment being cost-effective. Phase I and II trials provide early evidence on drug efficacy and tolerability and initial cost estimates. Based on value of information, cost-effectiveness and budget impact models, only drugs deemed to meet authority requirements would be selected. Market intelligence and uncertainties and clinical success probability further enable identification of the optimal portfolio containing drug candidates that maximize NPV for given risk levels. **CONCLUSIONS:** Health economic methods are commonly applied during late stage development, but if implemented alongside capital investment tools from earliest R&D stages they could increase the likelihood of selecting the right products to compose an effective investment portfolio.

**PRM237****MULTIVARIATE NETWORK META-ANALYSIS OF PROGRESSION FREE SURVIVAL AND OVERALL SURVIVAL**Jansen JP<sup>1</sup>, Trikalinos T<sup>2</sup><sup>1</sup>Mapi / Tufts University School of Medicine, Boston, MA, USA, <sup>2</sup>Brown University, Providence, RI, USA

Cancer treatment effectiveness is often quantified by analyzing time from treatment initiation to the occurrence of a particular event. Very commonly studies report data on overall survival (OS), where the event is death from any cause, and on progression-free survival (PFS), where the event is death from any cause or disease progression, whichever occurred first. Both OS and PFS can inform decision making. Separate meta-analyses of OS and of PFS data ignore the correlation between the outcomes. We introduce a method for the joint meta-analysis of OS and PFS that is based on a tri-state transition model with time-varying hazard rates modeled with fractional polynomials. In English, we assume that, at any time, patients can be in one of three health states: “alive but not progressed”, “alive and progressed”, and “dead”. PFS corresponds to time spent in the first state, and OS to time spent in the two alive states. The proposed approach allows the joint network meta-analysis of OS and PFS, relaxes the proportional hazards assumption, extends to a network of more than two treatments, and simplifies the parameterization of decision and cost-effectiveness analyses. The data needed to run these analyses can be extracted directly from published survival curves. We demonstrate use by applying the methodology to a network of trials for the treatment of non-small cell lung cancer.

**PRM238****USING LOWER COST, LOWER EFFICACY INTERVENTIONS CAN IMPROVE POPULATION HEALTH OUTCOMES UNDER BUDGET CONSTRAINTS**

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**BACKGROUND:** The global economic crisis imposes severe restrictions on budgets allocated to health care. Innovative technologies in medicine may improve patient outcomes but such improvements come at a substantial cost, thus limiting the number of patients that may benefit from them. According to current cost-effectiveness analyses (CEA), most innovative interventions are associated with a higher efficacy and higher costs compared with the standard of care. These analyses do not account for the budget impact associated with implementing the interventions on all eligible patients. Even when a new intervention is highly cost-effective, health care systems may not be able to adopt it due to substantial budgetary impacts. Implementing a substantially lower-cost intervention to a substantially wider population, accepting inferior per-patient outcomes, may improve overall health outcomes under a restricted budget. **OBJECTIVES:** Develop an innovative health technology assessment (HTA) model that combines CEA and budget-impact analyses, thus enabling to compare the impact of intervention alternatives on the entire intended use population, under a pre-specified budget constraint. **METHODS:** We identified the following steps to be included in the model formulation: 1) Define the intended use and the target population. 2) Define two or more interventions, one of them at higher cost and better per-patient outcome, and the second with lower cost and inferior per-patient outcome. 3) Forecast the diffusion of the alternatives into the entire intended use population, under a pre-defined budget, in order to estimate the treated and untreated populations. 4) Calculate the clinical impact of each alternative on the treated population. 5) Calculate the clinical impact of no therapy on the untreated population. 6) Compare the aggregated clinical impact of each alternative on the entire intended use population – both treated and untreated. Using the proposed population-based model may result in improved health care outcomes, especially in times of economic downturn and austerity.

**PRM239****EVIDENCE-BASED METHODS IN FOOD SCIENCES AND NUTRITION**Quignot N<sup>1</sup>, Amzal B<sup>2</sup><sup>1</sup>LA-SER Analytica, Paris, France, <sup>2</sup>LASER Analytica, London, UK

Evidence-based medicine has emerged as the bottom line of Health Technology Assessments for drug evaluations. Over the last decade, evidence-based assessment of food and nutritional products has accelerated. Specific quantitative tools to synthesize evidence have been increasingly developed, and used for decision support. This work aims at highlighting the critical role of systematic reviews and model-based evidence synthesis in the field of food sciences and nutrition, especially with the view of safety assessment. To first set the scene of food assessment in Europe, the latest Guidelines on Systematic Reviews published by the European Food Safety Authority (EFSA) (EFSA, 2010) are described with the approach on how to handle observational

data on the general population. Specific examples of large systematic reviews conducted for estimating food safety accounting for population variability and interactions between food contaminants and drugs are also presented. Details on the model-based meta-analyses of such safety data are described and discussed for the purpose of regulator's decision making. Systematic reviews have been to the context of food and nutritional epidemiology requiring more stringent quality assessment and more advanced management of variability. This resulted in a Bayesian random effect model accounting for population variability. Metabolic interactions between food and drugs were evidenced and variability metrics could be explicated in terms of “uncertainty factors” to be used by the food regulators to assess safety limits for food ingredients, contaminants or drugs and their combined use. Food regulator in EU is aligning and even sometimes anticipating drug regulators in terms of evidence-based safety assessment in the real life. Common tools for model-based evidence synthesis can be applied to quantify safety signals and interaction in the general population.

**PRM240****COMPARATIVE EFFICIENCY RESEARCH: META-ANALYSIS OF COST-EFFECTIVENESS STUDIES**Crespo C<sup>1</sup>, Monleon A<sup>1</sup>, Díaz W<sup>2</sup>, Rodriguez C<sup>1</sup>, Brosa M<sup>3</sup>, Rios M<sup>1</sup><sup>1</sup>University of Barcelona, Barcelona, Spain, <sup>2</sup>Universidad de Antioquia, Medellín, Colombia,<sup>3</sup>Oblique Consulting, Barcelona, Spain

**OBJECTIVES:** Cost-effectiveness analyses (CEA) have become widely used in several pathologies. Currently, new CEA studies comparing active vs control treatment have been incorporated each year. For this reason, the combination of CEA studies could give a more consistent and accurate estimate of an intervention's efficiency than one study alone. The aim of study was to develop a new method to do comparative efficiency research (COMER) based in individual patient data. **METHODS:** After, adjusted the marginal distribution and copula distribution of a hypothetical cohort, we stated the parameters and distribution estimated like our unknown theoretical distribution. We conducted an iterative analysis of a random Frank Copula distribution with a different range of sample size. We performed a comparison between samples and theoretical distribution in terms of incremental cost-effectiveness ratio (ICER), incremental monetary benefit (IMB) fixed a threshold ( $k = 20,000$  monetary units) and goodness of fit for Frank copula, assuming a tolerance. **RESULTS:** The Theoretical distribution fixed, showed a cost of 604.34 monetary units for active and 516.12 monetary units for control, and a utilities of 0.529 for active and 0.492 for control. ICER for theoretical cohort was 2,380 monetary units per quality-adjusted life year gained and IMB was 653. With a tolerance of 500 monetary units for ICER and 50 monetary units for IMB, only 15.52% of simulations were near the theoretical ICER and only 6.12% of IMB. The amount of individual patients simulated was more than 500 patients per treatment to fit Frank Copula. **CONCLUSIONS:** Preliminary results showed that COMER based in individual patients' data could allow decision maker to know real add-value of a new intervention.

**PRM241****EVALUATING THE ECONOMIC IMPACT OF TECHNOLOGICAL ADVANCES IN DIAGNOSTICS: THE CASE OF HIGH THROUGHPUT SEQUENCING FOR HEREDITARY BREAST CANCER**

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Benefits of diagnostics tests generally centre on test accuracy measures. However, additional benefits of diagnostics may include: reduced laboratory time, reduced time to results and increases in the capacity of a laboratory to deliver more tests. New technological developments, such as high throughput sequencing (HTS) are challenging the current methods used in establishing the case for the introduction into clinical practice terms of economic impact. This is evident in the case study developed here examining BRCA1/2 genetic testing in providing information on the risk of development of breast cancer. Current BRCA1/2 testing technologies are limited by long (up to one-year) turnaround times, which together with limited resources to increase the volume of tests and associated genetic counselling, has driven the use of a ‘risk threshold’ to target women eligible for testing. HTS offers the opportunity of decreased turnaround time and increased volume of BRCA1/2 tests, which will impact on the benefits and costs associated with the diagnostic service. Systematic reviews have identified Markov-type models as the dominant modeling methodology for the assessment of genetic testing. We propose that discrete event simulation (DES) is the appropriate model type to quantify the economic impact of HTS BRCA1/2 testing as it allows evaluation of the impact of capacity constraints and increased turnaround time on the costs and benefits of this new diagnostic technology. Importantly, DES also allows for the assessment of structural uncertainty by considering changes in patient pathways when using a new diagnostic technology. While DES may be the most appropriate modeling methodology in assessing the economic impact of novel genetic tests; typically the type of data and information required to populate these models is lacking. We conclude by highlighting the type of data required to both population appropriate models and to adequately assess the economic impact of these novel genetic tests.

**PRM242****THE IMPORTANCE OF SENSITIVITY ANALYSES IN HEALTH TECHNOLOGY ASSESSMENTS**

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In this paper, we critically evaluated analytical design of health technology assessment methodologies, particularly related to sensitivity analyses and willingness-to-pay thresholds. To this end, we have used two studies: the first one analyzing cost-effectiveness of a human papillomavirus vaccination of boys at age 12 against oropharyngeal carcinoma and anogenital warts and the second one examining cost-effectiveness of a universal programme of vaccinating children against pneumococcal disease. We have shown – as expected – that the impact of variation of parameters can be substantial, however, outcomes of sensitivity analyses are often understated both by marketing authorization holders and authorities. Few would